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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,586	10/27/2003	Ekambar R. Kandimalla	HYB-005US5	3762
7590 WAYNE A. KEOWN SUITE 1200 500 WEST CUMMINGS PARK WOBURN, MA 01801				
EXAMINER				
HORNING, MICHELLE S				
ART UNIT		PAPER NUMBER		
1648				
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10/29/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/694,586

Applicant(s)

KANDIMALLA ET AL.

Examiner

MICHELLE HORNING

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20, 21 and 41-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20, 21, 41-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The previous office action is vacated.

The status of the claims is as follows: claims 20, 21, 41 and 42-51 are under current examination.

The following rejection has been withdrawn due to persuasive arguments by Applicant:

1. 35 USC 103 (Chaix et al (1996), US Patent # 6562798 (Schwartz), Smee et al (1991) and Schneider and Chait (1995).

Claim Rejections - 35 USC § 103-MAINTAINED

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20-21, 42-44 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Chaix et al (1996) and US Patent # 6562798 (Schwartz). Note that new claims 42-44 and 48 are rejected for the reasons set forth below as necessitated by amendment.

Response to Arguments

Applicant's arguments filed 2/26/2008 have been fully considered but they are not persuasive. Applicant notes that Chaix et al relates to the antisense art and that there was no reason to expect that the introduction of a 3'-3' linkage would have any deleterious effect on antisense activity (see Remarks, page 6). In contrast, the claimed invention is drawn to oligonucleotide based immunostimulatory compounds and that only Applicant's specification establishes that accessible 3'ends were not required for immunostimulatory activity (Remarks, page 7). With respect to the insertion of 3'-3' linkers, Applicant requests a clarification of the recitation "this insertion would have been obvious for any oligonucleotide of any function".

Chaix et al provides the following: "the major pathway of degradation of normal and modified oligonucleotides is exonuclease-mediated and occurs from the 3'-end" (see page 828). While Chaix et al describes antisense oligonucleotides and the instant invention discloses immunostimulatory oligonucleotides, it is not clear how a nuclease would selectively degrade an oligonucleotide with an antisense function over an immunostimulatory function. The intended function of any sequence is compromised if its structural integrity is altered by nuclease degradation. Paragraph 114 of the instant specification also acknowledges this in the following statement: "It is important to note

that 3'-3'-linked oligos have shown substantially greater stability towards degradation by exonucleases than the oligos that contained a free 3'-end, which could also result in increased immunostimulatory activity." Thus, the applied motivation to insert a 3'-3' linker is to maintain the structural integrity of an oligonucleotide. With respect to the immunostimulatory activity of an oligonucleotide in the presence or absence of such linker, note that a molecule and its inherent properties are inseparable (see MPEP 2112.01). Given there is ample motivation to insert such a 3'-3' linker by the prior art as further evidenced by the instant specification, the rejection is maintained.

With respect to the new claims, the Schwartz provides an oligonucleotide compound comprising the dinucleotide C*pG wherein the C* is a cytidine analog. See Figure 1 depicting a 5-bromocytosine with the following characteristics: D is a hydrogen bond donor, D' is a bromide, A is a hydrogen bond acceptor, X is a carbon and S is a pentose. This non-natural cytidine or deoxycytidine is taught by Schwartz. Schwartz does not provide a 3'-3' linker.

Chaix et al discloses oligonucleotide sequences that include a 3'-3' linker and 2 accessible 5' ends (see Table 1). The authors disclose a marked increase in stability of these sequences due to the incorporation of the linker (see Conclusions). It would have been obvious to one of ordinary skill in the art to combine the teachings above and modify the oligonucleotide taught by Schwartz. One would have been motivated to do so, as taught by Chaix et al, in order to increase the oligonucleotide's stability against nuclease-mediated degradation in contrast to 5'-3' oligonucleotides. There would have been a reasonable expectation of success given the underlying techniques are

commonly used and widely known. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112-NECESSITATED BY AMENDMENTS

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Both claims depend from cancelled claims, 04 and 08. Note that at least 5-hydroxymethylcytosine and 5methylcytosine occur naturally by way of oxidative damage to phage and E. coli DNA.

Claim Rejections - 35 USC § 103-NECESSITATED BY AMENDMENTS

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42, 43, 46, 47, 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent # 6562798 (Schwartz) and US Patent 6365730 (Jennings).

Claims 42 and 43 are rejected as discussed above under the teachings of Schwartz. Schwartz provides an oligonucleotide compound that comprises a C*pG in which the C* is a modified cytidine. This reference does not teach using a non-naturally occurring sugar moiety.

Jennings teaches that nucleoside derivatives such as ribose pentoses, including arabinose, are resistant to nuclease attack (see paragraph 29). Thus, it would have been obvious to one of ordinary skill in the art to combine the teachings above and make the claimed invention. One would have been motivated to do so in order to prevent nuclease degradation as taught by Jennings of the C*pG containing-sequences provided by Schwartz. There would have been a reasonable expectation of success given the underlying techniques are widely known and commonly used. The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting-NECESSITATED BY AMENDMENTS

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 42-45, 48 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 7262286 in view of Chaix et al. The claims of US Patent No. 7262286 are drawn to the sequences containing the CpG motif wherein the cytidine may be modified including 5-hydroxycytosine, 5- hydromethylcytosine, N4-alkylcytosine or 4-thiouracil. US Patent No. 7262286 does not teach insertion of a 3'-3' linker within these sequences while the instant claims do. The teachings of Chaix et al discloses that incorporating a 3'-3' linker leads to a marked increase in sequence stability and this insertion of such a linker would have been obvious to one of ordinary skill in the art.

Allowable Subject Matter

Claim 41 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 45 and 49 are allowed with the exception of the Double Patenting rejection.

Conclusion

NO claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **MICHELLE HORNING** whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michelle Horning/
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648